



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,301	11/26/2003	Barbara Enenkel	I/1411	5533

28501 7590 03/08/2006

MICHAEL P. MORRIS
BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877-0368

EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
----------	--------------

1652

DATE MAILED: 03/08/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/724,301

Applicant(s)

ENENKEL ET AL.

Examiner

Malgorzata A. Walicka

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 February 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-54 is/are pending in the application.
- 4a) Of the above claim(s) 6-8, 10, 12-15, 16 in part, 17-23, 25-31 and 33-54 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3, 9, 11, 6 in part, 24 and 32 is/are rejected.
- 7) ☒ Claim(s) 4 and 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11/226/2003 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

The Response to Restriction filed Feb. 13, 2006 is acknowledged. Claims 1-54 are pending. The elected claims 1-5, 9, 11, 16 in part, 24 and 32 are under examination. Claims 6-8, 10, 12-15, 16 in part, 17-23, 25-31 and 33-54 are withdrawn from examiner's consideration as directed to a non-elected invention; see 37CFR 1.142 (b).

DETAILED ACTION

1. Restriction/election

Applicant's election with traverse of Group I claims Claim 1-5, 9, 11, 16 in part, 24, and 32, drawn to a neomycin phosphotransferase mutated in positions 91, 198 and /or 240, its encoding gene, expression vector, host cell, and a method of use of the vector for enriching of mammalian cell, classified in class 436, subclass 325 in the reply filed on Feb. 13, 2006 is acknowledged. The traversal is on the ground(s) that examination of the claims in Groups I-VI would not create an undue burden on the examiner, because all the groups are sufficiently related since each of these Groups involve a neomycin phosphotransferase and use thereof".

This is not found persuasive for the following reasons. The claims are directed to 9 mutants of E. coli neomycin phosphotransferase and their 9 encoding DNA sequences plus the wild type of the enzyme and the encoding gene. The claims are directed to the use of these 18 products a well! Furthermore group III is related to any neomycin phosphotransferase having the activity lower than its wild type. Groups I-III comprise several genes and enzymes expression vectors and one method of use of

Art Unit: 1652

said vector. Groups IV-VI are directed to a second use of the same group of genes and proteins as those in Groups I-III. According to the US restriction practice a second method of use of the claimed product is restricted. In addition, Applicants are kindly reminded that restriction involves four factors: distinctness, independence, classification and burden on the examiner. For reasons explained in the restriction requirement the inventions are distinct, independent and have different classification. Because all four factors are believed undisputable, in the light of the explanations in restriction requirement and discussion above, the restriction is proper and made FINAL. Elected Group I, claims 1-5, 9, 11, 16 in part, claim 24 and 32, drawn to a neomycin phosphotransferase mutated in positions 91, 198 and /or 240, its encoding gene, expression vector, host cell, and a method of use of the vector for enriching of mammalian cell, classified in class 436, subclass 325 is under examination. Claims 6-8,10, 12-5, 16 in part, 18-23, and 25-32 and 33-54 are withdrawn from examiner's consideration as directed to a non-elected invention; see 37CFR 1.142 (b).

2. Priority

Acknowledgment is made of Applicant's claim for priority based on German Patent applications 102 56 081, filed 11/29/2002 and 10330686, filed 7/08/2003. The priority to the German applications has not been granted, because the Applicants have not filled the English translations. The instant application also claims priority to the US provisional applications 60/431,535 and 60487,902 filed 12/6/2002 and 07/17/2003,

Art Unit: 1652

respectively. However, only the priority to application 60/435,535 has been granted because Applicants filed its English translation.

3. Objections

Claim 16 is objected as depending on the nonelected claim 14.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors in the specification of which applicant may become aware.

Fig 5 and 6 are objected to because description of the X-axis is in German.

4. Rejections

4. 1. 5 USC section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-3 and 9-11, 24 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim s 1-3 , 9-11are unclear as it is unclear what phosphotransferase gene they are referring to.

Art Unit: 1652

Claim 24, as written, does not sufficiently distinguish between isolated mammalian cells containing a modified neomycin phosphotransferase gene, i.e. a transformed cell in vitro, and a cell in the body of a transgenic animal.

Claim 32 is unclear because the preamble does not state what enrichment is referred to. In another words, as there are many features in the cells in vitro that can be selected for, Applicants must state in which cells the pool of transfected cells is to be enriched.

4.2. 35 USC section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4.2.1. Written description

Claims 1-3 and 9-11, 24 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims are directed to a modified neomycin phosphotransferase gene wherein said gene encodes the enzyme having amino acids positions 91 and/or, 198, and or 240 are modified. The claims are directed to a large and versatile genus of enzymes for which the disclosure

Art Unit: 1652

does not provide a sufficient description of structure. Applicants provide only examples of the genus of modified enzyme which has the wild type sequence set forth by SEQ ID NO: 2 (encoded by SEQ ID NO: 1) and is a wild type of E. coli neomycin phosphotransferase. Providing a single representative of the claimed genus does not provide a structural identifying characteristic of the whole genus, which encompasses any neomycin phosphotransferase, from any organism, or man made, wherein all the species of the genus have amino acids in positions 91, 198 or 240 changed.

Because Applicants failed to identify the claimed genus structurally, the claimed subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4-5 are objected to as depending on rejected claim 1.

4.2.2. Scope of enablement

Claims 1-3 and 9-11, 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for modified E. coli gene of SEQ ID NO: 1 (wild type) encoding neomycin transferase which is identified by SEQ ID NO: 2, does not reasonably provide enablement for any, i.e., all modified neomycin phosphotransferases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Art Unit: 1652

The scope of the claim must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)), otherwise, making and/or using the invention requires additional experimentation.

The factors to be considered in determining whether undue experimentation is required to make the invention are summarized In re Wands [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and the breadth of the claim.

The nature of the invention is any gene encoding a transferase having an amino acids positions 91, 198, and 240 (separately or in combination) changed in comparison with the wild type. The breadth of the scope covers any modified gene from any natural source; i.e., the breath of the claims covers all natural neomycin transferases that have their positions 91 and/or 198 and/or 240 changed and retain the desired activity.

While mutating genes of any protein is well known and skills of artisan high, it is possible to mutate particular positions of the amino acid sequence only when the gene/protein sequences are known. Providing SEQ ID NO: 2 mutated in positions 91, 198 and 240 is not sufficient for mutating the same positions in any neomycin phosphotransferase, because the sequences of all wild type amino acid phosphotransferases are not known in the art, and one having skills is the are does not known how to identify positions 91, 198 and 240 in the protein. Furthermore it is

Art Unit: 1652

uncertain that the change of the quoted amino acid residues is neutral for the protein activity in any neomycin phosphotransferase, as structure/function relationship for all neomycin transferases is not known.

While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed so that the claimed species have the functionality intended by Applicants. The provision of SEQ ID NO: 1 fails to provide such guidance of polynucleotides which are to be mutated to encode for all neomycin transferases having changes in positions 91, 198 and 240. Without a further guidance on the part of Applicants with regards to the structure of the wild type neomycin phosphotransferases to be changed the experimentation left to those skilled in the art is improperly extensive and undue.

Claims 4-5 are objected to as depending on the rejected claim 1.


In addition claim 32 is rejected, because the specification while Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka whose telephone number is (571) 272-0944. The examiner can normally be reached on Monday-Friday from 10:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1652

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Malgorzata A. Walicka, Ph.D.
Art Unit 1652
Patent Examiner



PONNATHAPACHUTAMURTHY
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1800